

**BUDGET ESTIMATES FOR ALL YEARS OF SUPPORT REQUESTED FROM PUBLIC HEALTH SERVICE
DIRECT COSTS ONLY (Omit Cents)**

DESCRIPTION		1ST PERIOD (SAME AS DE- TAILED BUDGET)	ADDITIONAL YEARS SUPPORT REQUESTED (This application only)					
			2ND YEAR	3RD YEAR	4TH YEAR	5TH YEAR	6TH YEAR	7TH YEAR
PERSONNEL COSTS		3,414	3,656	3,908	4,177	4,464		
CONSULTANT COSTS (Include fees, travel, etc.)		-	-	-	-	-		
EQUIPMENT		-	-	-	-	-		
SUPPLIES		-	-	-	-	-		
TRAVEL	DOMESTIC	-	-	-	-	-		
	FOREIGN	-	-	-	-	-		
PATIENT COSTS		-	-	-	-	-		
ALTERATIONS AND RENOVATIONS		-	-	-	-	-		
OTHER EXPENSES		5,000	5,300	5,700	6,000	6,400		
TOTAL DIRECT COSTS		8,414	8,956	9,608	10,177	10,864		
TOTAL FOR ENTIRE PROPOSED PROJECT PERIOD (Enter on Page 1, Item 4) →						\$ 48,019		

REMARKS: Justify all costs for the first year for which the need may not be obvious. For future years, justify equipment costs, as well as any significant increases in any other category. If a recurring annual increase in personnel costs is requested, give percentage. (Use continuation page if needed.)

Budget explanation attached

AGGREGATE BUDGET EXPLANATION

The following budget is the aggregate of the five individual subprogram budgets and the Program Director's Office budget. Individual budget items such as personnel appearing in more than one budget and supply items like "chemicals, glassware, etc." have been combined to show only one such item each in this overall budget.

In considering the percentages of personnel time committed to this project, it should be noted that faculty personnel, as distinct from staff, also receive a portion of their salary from the institution. This institutional salary support assists in covering faculty efforts along research lines overlapping those in the present application. Therefore the faculty time percentages reflect contractual lower bounds on faculty commitment to this program.

Salaries are uniformly increased at a rate of 6% per year to cover expected merit and cost of living increases. Staff benefits are applied based on the following University projections: 17%, 9/73-8/74; 18.3%, 9/74-8/75; 19.3%, 9/75-8/76; 20.3%, 9/76-8/77; 21.3%, 9/77-8/78; 22.3%, 9/78-8/79.

Budget items other than "Equipment" and "Patient Costs" are in general increased by 6% per year to cover inflation, except in specific instances noted in the individual budgets.

SUBSTITUTE DETAILED BUDGET FOR FIRST 12-MONTH PERIOD		PERIOD COVERED		GRANT NUMBER
		FROM 1/1/74	THROUGH 12/31/74	
1. PERSONNEL (List all personnel engaged on project)			TIME OR EFFORT %/HRS.	AMOUNT REQUESTED (Omit cents)
NAME (Last, first, initial)	TITLE OF POSITION			TOTAL
Lederberg, J.	Principal Investigator or Program Director	20	AGGREGATE PROGRAM BUDGET	
Cann, H.	Assoc. Prof. of Peds.	50		
Kretchmer, N.	Prof. of Peds.	10		
Herzenberg, L.	Prof. of Genetics	10		
Cavalli-Sforza, L.	Prof. of Genetics	10		
Barnett, C.	Assoc. Prof. of Peds.	20		
Luzzatti, L.	Prof. of Peds.	10		
Tsuboi, K.	Senior Scientist	20		
Duffield, A.	Research Associate	100		
Pereira, W.	Research Associate	100		
Rindfleisch, T.	Research Associate	20		
Hulett, H.	Research Associate	20		
Open - Genetics	Research Associate	100		
Open - Pediatrics	Research Associate	100		
(continued)				
TOTAL →				\$ 345,600
2. CONSULTANT COSTS (Include Fees and Travel)				\$
3. EQUIPMENT (Itemize)				
see attached				\$ 126,200*
4. SUPPLIES				
see attached				\$ 35,700
5. STAFF TRAVEL (See Instructions)	a. DOMESTIC 7 East Coast(3,500), 1 Mid-west (300), 1 West Coast(200)			\$ 4,000
	b. FOREIGN			\$
6. PATIENT COSTS (Separate Inpatient and Outpatient)				
Venepuncture (500) and genetic counseling (2,500)				\$ 3,000
7. ALTERATIONS AND RENOVATIONS				
Relocate equip., power, etc. for GC/MS data system				\$ 1,800
8. OTHER EXPENSES (Itemize per instructions)				
see attached				\$ 21,500
9. Subtotal - Items 1 thru 8 →				\$ 537,800
FOR TRAINING GRANTS ONLY	10. TRAINEE EXPENSES (See Instructions)			
	a. STIPENDS	PREDOCTORAL	No. Proposed _____	\$
		POSTDOCTORAL	No. Proposed _____	\$
		OTHER (Specify)	No. Proposed _____	\$
		DEPENDENCY ALLOWANCE		\$
	TOTAL STIPEND EXPENSES →			\$
	b. TUITION AND FEES			\$
c. TRAINEE TRAVEL (Describe)			\$	
11. Subtotal - Trainee Expenses →			\$	
12. TOTAL DIRECT COST (Add Subtotals, Items 9 and 11, and enter on Page 1) →				\$ 537,800

continued

1. PERSONNEL	TITLE	% TIME
Open	Research Assoc.-Stat.	20
Open - Pediatrics	Research Assoc. - Soc. Worker	50
Veizades, N.	Research Engineer	33
Steed, E.	Research Engineer	33
Tucker, R.	Computer Programmer	75
Wegman, A.	Senior Res. Assist.	10
Waters, R.	Research Assist.	100
Sakaguchi, S.	Research Assist.	50
Van West, B.	Research Assist.	100
Makk, G.	Research Assist.	100
Open - Pediatrics	Research Assist.	50
Summons, R.	Post.Doc. Fellow	100
Open - Genetics	Grad. Res. Assist.	50
Open - Genetics	Grad. Res. Assist.	50
Pearson, D.	Electronics Tech.	40
Wyche, M.	Lab. Tech.	100
Boswell, M.	Lab. Tech.	100
Open - Genetics	Engin. Tech.	50
Open- - Genetics	Research Tech.	100
Open - Pediatrics	Interviewer	50
Open - Pediatrics	Interviewer	25
Open - Pediatrics	Statist. Clerk	50
Open - Pediatrics	Data Coder	65
Jamtgaard, R.	Administrator	15
Redse, R.	Secretary-Prog.Dir.	30
Allen, M.	Secretary - IRL	25
Murray, R.	Secretary - Peds.	50
Meyering, P.	Secretary - Gen.	10
Open - Pediatrics	Typist	100
Harlow, W.	Machinist	10
Cusumano, M.	Laboratory Diener	50
Open - Genetics	Lab Glasswasher	25

continued

3. EQUIPMENT

4 Column Gas Chromatograph	\$14,400*
Mini-computer System & Inst. Interface	59,900*
Amino Acid Analyzer	32,500*
Event Counter	2,700*
Digital Voltmeter	900*
Carbon Dioxide Incubator	2,500*
Laminar Flow Hood	1,000*
Fluorescence Microscope	9,000*
Eppendorf Microfuge	500*
Buchler Power Supply	600*
Constant Current Power Supply	1,000*
Slab Gel Electrophoresis	300*
Column Acrylamide Gel Electrophoresis	200*
Destainer	200*
Tape Recorder	500*

Total Equipment \$126,200*

4. SUPPLIES

Chemicals, glassware & lab. apparatus	\$18,000
GC Supplies (Columns, Phases, etc.)	1,100
Dry ice & liquid nitrogen	500
Data recording media (GC/MS, Calcomp, etc.)	1,800
Mini-computer supplies (start-up & continuing)	1,600
Mass spectrometer repair parts & supplies	2,300
Electronic parts & supplies	1,900
Amino acid analyzer supplies	2,000
Radioactive tracers	5,000
Expendable supplies (photo. plates, etc.)	1,500

Total Supplies \$35,700

8. OTHER

Visiting committee honoraria & expenses for annual symposium	\$5,000
Office supplies, telephone, repor., postage, publication costs, etc.	6,200
Mini-computer maintenance	6,000
Freight on capital equipment	500
Central computer usage & terminal rental	3,800

Total Other \$21,500

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			2ND YEAR	3RD YEAR	4TH YEAR	5TH YEAR	6TH YEAR	7TH YEAR
PERSONNEL COSTS		\$345,600	370,068	431,528	461,243	492,966		
CONSULTANT COSTS (Include fees, travel, etc.)								
EQUIPMENT		126,200*	23,000*	18,100*	5,300*	6,000*		
SUPPLIES		35,700	37,700	42,400	44,800	47,700		
TRAVEL	DOMESTIC	4,000	4,700	4,900	4,900	5,400		
	FOREIGN							
PATIENT COSTS		3,000	5,500	5,500	500	500		
ALTERATIONS AND RENOVATIONS		1,800						
OTHER EXPENSES		21,500	24,900	26,400	27,800	29,700		
TOTAL DIRECT COSTS		537,800	465,868	528,828	544,543	582,266		
TOTAL FOR ENTIRE PROPOSED PROJECT PERIOD (Enter on Page 1, Item 4) —————→						\$ 2,659,305		

REMARKS: Justify all costs for the first year for which the need may not be obvious. For future years, justify equipment costs, as well as any significant increases in any other category. If a recurring annual increase in personnel costs is requested, give percentage. (Use continuation page if needed.)

See individual subprojects for budget explanations

SECTION VIII

Concluding Remarks

Dr. Lederberg

CONCLUDING REMARKS

(Joshua Lederberg)

The overt justification for the proposed Center is, of course, the collective value of the well-defined research projects that will make up its day to day work. However, its most important utility in the long run may be a new institutional arrangement that will generate now unforeseen lines of investigation. Molecular biology as a basic science has leaped far beyond its practical application to human problems. The more intimate intellectual association of gifted scientists and clinicians envisaged here, the development of an active interface among workers who spend much of their time still either in basic laboratory work or in the clinic, is the only possible way of advancing these applications.

Speaking more personally, I can point to a number of anticipations from my own research career that might have been explored more aggressively had I then pressed them in an interdisciplinary context. My early work (with Tatum, Zinder and others) on genetic recombination and on viral transduction in bacteria was foreseen years ago as laying a groundwork for the development of a genetics of somatic cells and of means of importing reparative genetic information ("genetic engineering"). Subsequently, I tried to stress that the new molecular genetics would overtake other lines of concern about genetic impairment, and improvement, and that ethical issues would loom as large as technological opportunities in public policy debates. While public reactions to these potentialities are in some respect overdrawn, geneticists obviously must inculcate and exhibit great sensitivity to the ethical issues of genetic intervention and how they are perceived by the public (1).

Although much of my own laboratory research might go under the heading of genetic engineering of bacteria (2) I have been persuaded that prenatal diagnosis represents the most important practical avenue of genetic therapy or rather pre-emption of disease. For this reason, the application of automated technologies (growing in large measure out of NASA-supported work) is emphasized in this application.

What is more difficult to foresee is the intensive development of the whole repertoire of tools of molecular genetics. Somatic cell genetics is well launched; but we will surely also have to learn how to use specific DNA replication, hybridization, transcription, and translation, i.e. the full range of gene action in vitro, to solve pressing diagnostic problems.

Laboratory research shares a place with other interests. I can summarize these under the heading of a concern for the overall process of science, and its application for human benefit. These meta-scientific interests have been expressed in the public arena, as in efforts to enhance public understanding of science and provision for its support. More recently, I have been more involved in efforts to enhance the infrastructure of science, with work on new instrumentation coupled with feeble steps towards the use of computers for scientific "intelligence" (3).

The Genetics Research Center is a plan to bring all of these themes to a focus on an area most likely to advance genetic knowledge -- my fundamental scientific base -- and to generate tangible health benefits for the mutual advantage of both disciplines, and to satisfy the public's motives for continued investment in the health sciences.

Bibliography

1. Lederberg, J.: in Challenging Biological Problems, Oxford U. Press, N.Y. 1972, p. 7 (J.A. Behnke, ed.) "Biological Innovation and Genetic Intervention".
2. Sgaramella, V.: Proc. Nat. Acad. Sci. 69:3389, 1972.
"Enzymic Oligomerization of Bacteriophage P22 DNA and of Linear Simian Virus 40 DNA."
3. Lederberg, J.: in Biochemical Applications of Mass Spectrometry, John Wiley & Sons, N.Y. 1972, p. 193 (G.R. Waller, ed.) "Use of a Computer to Identify Unknown Compounds: The Automation of Scientific Inference."

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SECTION IX

Professional Personnel

KEY PERSONNEL AND BIOGRAPHICAL MATERIAL

Joshua Lederberg, Ph.D. - Principal Investigator, Professor and Chairman, Department of Genetics.

Professor Lederberg will serve as the Principal Investigator for the overall program, and for part 1, automated screening methods (GC/MS) for inborn errors of metabolism. In addition, Professor Lederberg maintains active research programs in genetic recombination in bacteria; mechanisms of DNA replication and reunion; interactions of environmental mutagens with DNA; and computer emulation of human cognitive processes.

Howard Cann, M.D. - Associate Program Director, Associate Professor of Pediatrics.

Dr. Cann will assume responsibility for coordinating laboratory research with clinical applications within the program. This will involve screening of patients for their suitability of participation in the relevant research projects, obtaining appropriate patients for projects, informing patients about the research projects and obtaining their consent for participation, insuring that proper evaluation, care and counseling are provided to patients and families involved in these projects and planning for the application of the research findings to patient care. Dr. Cann will be directly involved with research projects on genetic markers in amniotic fluid, separation of fetal cells from the maternal circulation, the impact of genetic counseling on family decisions and screening and detection of inborn errors of metabolism. Dr. Cann's research activities pertain to human polymorphisms and to somatic cell genetics and his clinical work involves him with hereditary illness and genetic counseling. He has set up and directs a laboratory for typing for various polymorphisms of erythrocyte antigens and enzymes and serum proteins. He has initiated an investigative program for applying somatic cell hybridization to prenatal diagnosis of hereditary disorders.

L.L. Cavalli-Sforza, M.D. - Professor of Genetics

The investigations of Professor Cavalli-Sforza have long contributed and continue to contribute important information on human population genetics. He has pioneered in applying demography to studies of population and genetic structure of man. Particularly pertinent to this program is his interest and work on variation among populations in the frequency of inherited disorders and their determining genes.

Professor Cavalli-Sforza also directs a laboratory program oriented toward the detection of specific binding proteins in

blood. The detection of genetic polymorphisms of these proteins will be carried out by Professor Cavalli-Sforza as a research activity of this Genetics Center.

Norman Kretchmer, M.D., Ph.D. - Professor of Pediatrics.

Professor Kretchmer will participate in the research project dealing with screening and detection of inborn errors of metabolism. He is well known for his research and clinical work in various inborn errors of metabolism. One of Professor Kretchmer's main research interests presently deals with lactase intolerance in man. His research program also involves the developmental biochemistry of the urea cycle and the pyrimidine biosynthetic pathway in eukaryote cells and tissues. He has recently relinquished the chairmanship of the faculty committee for teaching the human biology curriculum at Stanford University. From 1959-1969 Professor Kretchmer was Chairman of the Department of Pediatrics.

Leonard Herzenberg, Ph.D. - Professor of Genetics.

Professor Herzenberg directs an active research program in immunogenetics with special emphasis on genetic and structural studies of mouse immunoglobulins and on the mechanism and control of antibody synthesis. The development under his direction of instrumentation for separating cells by means of fluorescent sensing has provided potential methodology for separating fetal cells from the maternal bloodstream. Professor Herzenberg will participate in the project which will apply this methodology to antenatal diagnosis of genetic disorders.

Clifford Barnett, Ph.D. - Professor of Anthropology and Associate Professor of Pediatrics.

Professor Barnett has worked in medical anthropology for 10 years. His research activities have dealt with cultural and genetic aspects of congenital dislocation of the hips, fertility and birth spacing of partially acculturated Guatemalan Indians, and mother and infant interactions in reference to premature infants. He has designed and will direct the research project on the impact of genetic counseling on family decisions and behavior.

Alan Duffield, Ph.D. - Research Associate in Genetics.

Dr. Duffield is an organic chemist who has carried out fundamental studies in mass spectrometry of organic compounds. He is presently directing research involving the development of a multicomponent, automated system for analysis of biologic substances. He shall apply this system, which involves a gas liquid chromatograph, a mass spectrometer and computer

facilities to screening, detecting, and studying inborn metabolic errors in various body fluids and tissues.

Kenneth Tsuboi, Ph.D. - Senior Scientist, Department of Pediatrics.

Dr. Tsuboi's research interests have included the physiological chemistry and enzymology of erythrocyte intermediate metabolism and more recently, the biochemical genetics of various erythrocyte enzymes. He is also working on the enzymological characteristics of various primate cell culture lines. In this program he will participate in the project on linkage and prenatal diagnosis of inherited disorders. In particular, he will work in the detection of polymorphic enzyme markers in cultured amniotic fluid cells.

Luigi Luzzatti, M.D. - Professor of Pediatrics.

Professor Luzzatti is the director of the clinical cytogenetics laboratory and of the Birth Defects Clinics in the Department of Pediatrics. His clinical activities which are pertinent to this program, include comprehensive care for patients (and their families) with birth defects, genetic counseling and screening amniotic fluid samples (usually from women over 35 years of age) for chromosomal abnormalities. He will participate in the project which investigates the impact of genetic counseling on family decisions.

Herbert Schwartz, M.D. - Professor of Pediatrics.

Professor Schwartz's research interests in hemoglobin synthesis, structures and function in health and disease, and their application to the prenatal detection of hereditary disorders involving hemoglobin, e.g. sickle cell anemia and thalassemia, will be incorporated into the program on exploring the maternal bloodstream for fetal cells. Dr. Schwartz will collaborate with Drs. Herzenberg and Cann in preliminary studies of fetal erythrocytes separated from maternal blood. Dr. Schwartz directs the hematology service of the Department of Pediatrics.

Other members of the Department of Genetics who will not participate directly in this program but with whom we interact daily are Dr. Eric Shooter (Professor) and Dr. A.T. Ganesan (Associate Professor). Professor Shooter directs research into the structure and mechanism of action of the nerve growth factor protein. Dr. Ganesan is investigating the genetic control of chromosome replication in *B. subtilis*, the chemical basis of DNA replication, the mechanism of genetic recombination during DNA mediated transformation and the role of the nuclear membrane in chromosome replication in mammalian cells.

The clinical and research interests of Professor Irving Schulman, Chairman of the Department of Pediatrics, are devoted to various defects of coagulation, including inherited disorders. Other members of the Department of Pediatrics whose clinical and research activities relate to this program are Dr. Phillip Sunshine (Associate Professor of Pediatrics) and Dr. John Johnson (Assistant Professor of Pediatrics), Director and Associate Director of the Newborn and Premature Infant Nurseries, respectively. Dr. Sunshine and Dr. Johnson are together investigating the metabolic consequences of neonatal ornithine transcarbamylase deficiency and detection of heterozygotes for the gene which determines this disorder. The research activities of Dr. Merton Bernfield, Associate Professor of Pediatrics, are designed to assess the morphogenetic behavior and cell surface properties of human cells and to utilize these assessments in studies of cells derived from individuals with birth defects. Dr. John Gribble, Assistant Professor of Pediatrics, is a pediatric hematologist whose research activities have dealt with in vitro biosynthesis of hemoglobin and biochemical and physiological aspects of pinniped hemoglobins. Dr. Gribble's clinical activities involve evaluation and treatment of patients with hereditary disorders of blood coagulation, including genetic counseling of their families. The clinical and research activities of Dr. R.O. Christiansen (Assistant Professor of Pediatrics and Director of the Pediatric Metabolic and Endocrine Service) and Dr. Judith Koehler (Assistant Professor of Pediatrics and Director of Pediatric Neurology) are quite relevant to the Genetics Center program. Even though the research activities of all of these individuals will not be supported by this grant, we are including bibliographic sketches on each of them because of their relevance to the overall Genetics Center program.

Within one or two years after the activation of this program we anticipate the direct participation of one or more colleagues from the Department of Obstetrics and Gynecology. A search for chairman of this department is presently under way, and we expect that this individual will bring competence to Stanford in fetal physiology and fetal monitoring. We look forward to interacting in this program with our obstetrical colleagues in various projects pertaining to antenatal detection of genetic disorders and selective abortion.

Research Support Summary for Departments of Genetics and Pediatrics
Relevant to Genetics Research Center

Program Director: J. Lederberg
Associate Program Director: H. Cann

Principal Investigator: (unless otherwise noted)	Grant Title	Current Year	Total Award	Grant Term	Budgeted % time
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HOWARD CANN
Associate Professor of Pediatrics
Department of Pediatrics

1) NIH:HL-15008	Pre-Natal Detection of Sickle Cell Anemia	\$ 38,717	\$118,000	9/72-8/75	
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LUCA CAVALLI-SFORZA
Professor of Genetics
Department of Genetics

1) AEC:AT-04-3-326	Mutation Rates and Mutational Loads in Man	32,000	32,000	10/72-9/73 (Renewal pending)	10%
2) NIH:NS-10711	Genetic Study of Metabolism of Neural Transmitters	65,000	207,000	9/72-8/75	20%
3) NIH:GM-20467	Gene Diffusion, Natural Selection and Drift in Man	47,587	147,351	5/73-4/76	20%

ADAYAPALAM GANESAN
Associate Professor of Genetics
Department of Genetics

1) NIH:GM50,199	Development Award-Research Career Program Chromosome Replication, Recombination and Cell Division	21,433	Support recommended for 2 additional years ending 12/31/75, the amounts to be determined annually.		
2) NIH:GM14108	DNA Synthesis and Genetic Recombination	34,902	211,996	6/72-5/77	50%

LEONARD HERZENBERG
Professor of Genetics
Department of Genetics

1)	NIH:GM-17367	Automated Cell Sorting - Clinical and Biological Uses	160,802	585,977	1/73-12/75	15%
2)	NIH:AI-08917	Genetics of Immunoglobins	52,774	246,386	5/69-4/74	20%
3)	NIH:CA-04681	Genetic Studies of Mammalian Cells	80,994	424,981	9/72-8/77	30%
4)	NIH:HD-01287	Fetal-Maternal Immunological Interactions	38,198	222,897	5/73-4/78	10%

JOHN D. JOHNSON
Assistant Professor
Department of Pediatrics

1)	United Cerebral Palsy	Developmental Aspects of Heme Protein Catabolism	28,772	53,322	7/71-6/73	
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NORMAN KRETCHMER
Professor of Pediatrics
Department of Pediatrics

1)	NIH:RR-00081	Clinical Research Center for Premature Infants	418,532	1,974,008	10/69-9/74 (Renewal pending)	5%
2)	NIH:HD-02147	Biochemical Studies of Development	206,593	1,309,278	6/66-5/74 (Renewal pending)	15%
3)	National Found. CRBS-252	Growth and Differentiation of the Placenta	23,293	23,293	7/72-6/74	15%
4)	NIH:HD-00047	Human Development and Pediatrics Training Grant	90,588	448,936	7/70-6/74	10%
5)	NIH:HD-00391	Regulation of Enzyme Action During Development	42,289	183,822	9/68-8/73 (Renewal pending)	15%

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NORMAN KRETCHMER (continued)

6)	NIH:CA14917	Pyrimidine Synthesis and Cellular Proliferation in Colon	42,689	130,737	6/73/5/76	20%
7)	Educational Found. of America	Epidemiology, Etiology, and Physiology of Diarrhea in the American Indian	45,156	92,915	7/73-6/75 (Renewal pending)	5%

JOSHUA LEDERBERG
Professor and Chairman
Department of Genetics

1)	NASA:NGR-05-020	Cytochemical Studies of Planetary Micro-organisms	180,000	3,800,000	9/60-8/73 (Future support dubious)	11%
2)	NIH:AI-05160	Genetics of Bacteria	60,000	280,000	9/68-8/73 (Renewal pending)	15%
3)	NIH:RR-00612	Resource Related Research - Computers and Chemistry (E. Feigenbaum, Principal Investigator; J. Lederberg and C. Djerassi, Co-Investigators)	194,408	675,000	5/71-4/74 (Renewal pending)	0%
4)	NIH:RR-00785	Stanford University Medical Experimental Computer Facility (SUMEX)	765,573	4,246,621	8/73-7/78 (pending)	20%
5)	NIH:GM0295	Training Grant in Genetics	143,964	756,650	7/69-6/74	15%

GILDA LOEW
Research Associate
Department of Genetics

1)	NSF:GB17980	Quantum Chemical Investigations of Heme Proteins and Ferredoxins	34,799	34,799	2/72-1/74 (Renewal pending)	50%
2)	NIH:DA00770	Quantum Chemical Studies of Opiate Narcotics	57,557	184,139	9/73-8/76 (Pending)	50%

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ERIC M. SHOOTER
Professor of Genetics
Department of Genetics

1)	NIH:NS04270	Molecular Neurobiology - Proteins in the Nervous System	84,558	404,979	12/70-11/75	40%
2)	NSF:GB31982	Structure and Mechanism of Action of the Nerve Growth Factor	60,000	60,000	1/72-12/73	20%

KENNETH TSUBOI
Senior Scientist
Department of Pediatrics

1)	NIH: Contract- Div. of Biol. Standards	Biochemical Parameters of Primate Cell Cultures	23,598	47,196	6/72-5/74	
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BIOGRAPHICAL SKETCH

(Give the following information for all professional personnel listed on page 3, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)

NAME Clifford R. Barnett	TITLE Associate Professor of Pediatrics Professor of Anthropology	BIRTHDATE (Mo., Day, Yr.) 8/17/29	
PLACE OF BIRTH (City, State, Country) New York, New York	PRESENT NATIONALITY (If non-U.S. citizen, indicate kind of visa and expiration date) U.S. Citizen	SEX <input checked="" type="checkbox"/> Male <input type="checkbox"/> Female	
EDUCATION (Begin with baccalaureate training and include postdoctoral)			
INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	SCIENTIFIC FIELD
The City College, New York, New York	B.S.S.	1950	Anthropology-Psychology
Cornell University, Ithaca, New York	M.A.	1951	Anthropology
Cornell University, Ithaca, New York	Ph.D.	1960	Anthropology
HONORS Executive Board, Society for Applied Anthropology 1967-70, Vice-President, 1971-72, President 1972-73, Past President 1973-74; Executive Board, Society for Medical Anthropology 1971-73; Chairman, Committee on Ethics, American Anthropological Association, 1971-74; Fellowship recipient, Milbank Memorial Fund, 1971-72.			
MAJOR RESEARCH INTEREST Cultural Anthropology		ROLE IN PROPOSED PROJECT Investigator	

RESEARCH SUPPORT (See instructions)

Research Grant: Genetic Studies in the Lake Atitlan Basin, Guatemala, GM 15593; \$14,130 for the current year; \$300,000 for the six year period 1967 - 1973; National Institutes of Health. Howard M. Cann, M.D. - principal investigator.

RESEARCH AND/OR PROFESSIONAL EXPERIENCE (Starting with present position, list training and experience relevant to area of project. List all or most representative publications. Do not exceed 3 pages for each individual.)

- 1964- Associate to Full Professor, Anthropology; Associate Professor, Pediatrics, Stan. Uni
- 1964-1970 Assistant Director to Acting Director, Program in Medicine and the Behavioral Sciences, Stanford University.
- 1962-1964 Research Associate to Associate Project Director, Navajo-Cornell Field Health Research Project, Dept. of Public Health, Cornell Univ. Medical College.
- 1961-1963 Resident Anthropologist, Navajo-Cornell Field Health Research Project at Many Farms, Arizona; Resident in Professional Practice, Russell Sage Foundation.
- 1955-1961 Senior Research Associate to Team Chairman, Foreign Areas Studies Division of Special Operations Research Office of the American University, Washington, D.C.

Publications (selected)

- "Untreated Congenital Hip Disease: A Study of the Epidemiology, Natural History and Social Aspects of the Disease in a Navajo Population". With D. Rabin, W. Arnold, R. Freiburger and G. Brooks. Supplement, American Journal of Public Health 55, 2. 1965.
- "Genetics of Diego Blood Groups in Guatemalan Indians: Use of Antiserums to Diego a and Diego b Antigens". With Howard M. Cann and Betty Van West. Science, 162:1391, 1968.
- "Neonatal Separation: The Maternal Side of Interactional Deprivation". With P.H. Leiderman, R. Grobstein, M. Klaus. Pediatrics 45:197, 1970.

(publications continued)

Publications (continued)

- "Child Spacing in a Highland Guatemala Community". With Jean Jackson and Howard M. Cann. In Culture and Population: A Collection of Current Studies, Polgar, (Ed.). Monograph 9, Carolina Population Center, Chapel Hill, 1971. pp. 139-148.
- "Health Care Experiment at Many Farms". With W. McDermott and K. Deuschle. Science 175:4017, January 7, 1972, pp. 23-31.
- "The Effects of Denial of Early Mother-Infant Interaction on Maternal Self-Confidence". With M. Seashore, A. Leifer and P. Leiderman. Child Development 43:1203, 1972.
- "Effects of Mother-Infant Separation on Maternal Attachment Behavior". With A. Leifer, P. Leiderman and J. Williams. In Press, Personality and Social Psychology.

BIOGRAPHICAL SKETCH

(Give the following information for all professional personnel listed on page 3, beginning with the Principal Investigator. Use continuation pages and follow the same general format for each person.)

NAME Merton R. Bernfield	TITLE Associate Professor	BIRTHDATE (Mo., Day, Yr.) April 9, 1938
PLACE OF BIRTH (City, State, Country) Chicago, Illinois	PRESENT NATIONALITY (If non-U.S. citizen, indicate kind of visa and expiration date) U.S.A.	SEX <input checked="" type="checkbox"/> Male <input type="checkbox"/> Female

EDUCATION (Begin with baccalaureate training and include postdoctoral)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	SCIENTIFIC FIELD
University of Illinois, Urbana, Illinois	B.S.	1959	Medicine
Graduate Division, University of Illinois, Chicago, Illinois	M.S.	1961	Biochemistry
College of Medicine, Univ. of Illinois, Chi.	M.D.	1961	

HONORS

Alpha Omega Alpha, 1959
Borden Undergraduate Research Award in Medicine
C.V. Mosby Company Research Award
Ross Award for Pediatric Research, 1971

MAJOR RESEARCH INTEREST

Developmental Biochemistry

ROLE IN PROPOSED PROJECT

Investigator

RESEARCH SUPPORT (See instructions)

NIH GM-15086-05 Ribonuclease and Oligoribonucleotide Synthesis, September 1, 1970 to August 30, 1975. Current year \$26,816. Total \$140,381.

NIH HD 06763 Extracellular Materials and Embryonic Organ Formation, May 1, 1972 - April 30, 1977. Current year \$45,401. Total \$203,648.

National Foundation-March of Dimes R-73-146 Morphogenetic Behavior of Human Cells July 1, 1973 - June 30, 1974. Total \$40,000.

RESEARCH AND/OR PROFESSIONAL EXPERIENCE (Starting with present position, list training and experience relevant to area of project. List or most representative publications. Do not exceed 3 pages for each individual.)

1970 - Associate Professor, Department of Pediatrics, Stanford University School of Medicine; Stanford, California

1970 - Co-Director, Medical Scientist Training Program, Stanford University School of Medicine; Stanford, California.

1969-1970 Associate Director, Medical Scientist Training Program, Stanford University School of Medicine; Stanford, California

1967 - Director, Birth Defects Research Center; Associate Director, Birth Defects Clinic, Department of Pediatrics, Stanford University School of Medicine; Stanford, California

1967-1970 Assistant Professor, Department of Pediatrics, Stanford University School of Medicine; Stanford, California

1967-1967 Chief Resident, Department of Pediatrics, Stanford Medical Center, Stanford

1965-1966 Research Investigator, National Institute of Child Health and Human Development with Dr. Clifford Grobstein, in the Department of Biology, University of California, San Diego; La Jolla, California

1963-1965 Research Associate, National Heart Institute, with Dr. Marshall Nirenberg; Bethesda, Maryland

1962-1963 Assistant Resident, Department of Pediatrics, New York Hospital-Cornell Medical Center; New York, New York

1961-1962 Rotating Internship, Research and Education Hospitals, University of Illinois Chicago, Illinois

Biographical Sketch of Dr. Merton Bernfield

Page Two, continuation of page one

Publications

- Bernfield, M.R. and Nirenberg, M.W.: RNA Codewords and Protein Synthesis. IV. The nucleotide sequences of multiple codewords for phenylalanine, serine, leucine, and proline. *Science* 147, 479-484, 1965.
- Bernfield, M.R. and Rottman, F.M.: Ribonuclease and Oligoribonucleotide Synthesis. III. Oligonucleotide synthesis with 5'-substituted uridine 2', 3'-cyclic phosphates. *J. Biol. Chem.* 242, 4134-4143, 1967.
- Maenpaa, P.H., and Bernfield, M.R.: Quantitative Variation in Serine Transfer Ribonucleic Acid during Estrogen-Induced Phosphoprotein Synthesis in Rooster Liver. *Biochemistry* 8, 4926-4935, 1969.
- Bernfield, M.R.: Collagen Synthesis during Epitheliomesenchymal Interactions. *Develop. Biol.* 22, 213-231, 1970.
- Bernfield, M.R., and Wessells, N.K.: Intra- and Extracellular Control of Epithelial Morphogenesis. *Develop. Biol. Supplement* 4, 195-249, 1970.
- Bernfield, M.R., Banerjee, S.D., and Cohn, R.H.: Dependence of Salivary Epithelial Morphology and Branching Morphogenesis upon Acid Mucopolysaccharide-Protein (Proteoglycan) at the Epithelial Surface. *J. Cell. Biol.*, 52, 674-689, 1972.

NAME Howard M. Cann, M.D.		Associate Professor of Pediatrics March 31, 1929
PLACE OF BIRTH (City, State, Country) Chicago, Illinois	PRESENT NATIONALITY (If non-U.S. citizen, indicate kind of visa and expiration date) U.S. Citizen	SEX <input checked="" type="checkbox"/> Male <input type="checkbox"/> Female

EDUCATION (Begin with baccalaureate training and include postdoctoral)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	SCIENTIFIC FIELD
University of Colorado, Colorado	B.A.	1950	Chemistry, Cum Laude (General Studies)
University of Colorado School of Medicine, Colorado.	M.D.	1954	

HONORS
 1971 - 1972 National Institutes of Health Special Research Fellowship, Genetics Laboratory, Department of Biochemistry, University of Oxford, England.
 1966 - 1971 Scholar in Academia Medicine, The John and Mary R. Markle Foundation.

MAJOR RESEARCH INTEREST	ROLE IN PROPOSED PROJECT (Continued on Page --)
Human Somatic Cell Genetics	ASSOCIATE INVESTIGATOR

RESEARCH SUPPORT (See instructions)

Research Grant: Genetic Studies in the Lake Atitlan Basin, Guatemala, GM 15593; \$28,260. for the current year; \$300,000. for the six year period 1967 - 1973; 35% effort; National Institutes of Health.
 National Institutes of Health Special Research Fellowship for sabbatical leave at the University of Oxford (Professor Walter F. Bodmer), Genetic Control of Human Transplantation Antigens, 1-FO3, HD51401-01; \$12,371. for one year, September 1, 1971 - August 31, 1972, 100% effort.

RESEARCH AND/OR PROFESSIONAL EXPERIENCE (Starting with present position, list training and experience relevant to area of project. List all or most representative publications. Do not exceed 3 pages for each individual.)

September 1, 1971 - August 31, 1972 National Institutes of Health Special Research Fellowship, Genetics Laboratory, Department of Biochemistry, University of Oxford, England.
 1970 - Associate Professor, Department of Pediatrics, Stanford University School of Medicine.
 1964 - 1970 Assistant Professor of Pediatrics, Stanford University School of Medicine
 1963 - 1964 Instructor, Department of Pediatrics, Stanford University School of Medicine.
 1962 - 1963 National Science Foundation Senior Postdoctoral Fellow, Institute of Genetics, University of Pavia, Pavia, Italy.
 1960 - 1962 Postdoctoral Fellow, Department of Genetics, Stanford University School of Medicine, Palo Alto, California.
 1957 - 1960 United States Public Health Service, Washington, D.C., Director, National Clearinghouse for Poison Control Centers. Draft Classification: 4A.
 1956 - 1957 Assistant Resident and Senior Resident in Pediatrics, Stanford University Hospital, San Francisco, California.
 1955 - 1956 Assistant Resident in Pediatrics, University of Colorado Medical Center, Denver, Colorado.
 1954 - 1955 Rotating Intern at San Francisco Hospital, University of California Service, San Francisco, California.

Committees and Consultant

- 1968 - Committee on Drugs, American Academy of Pediatrics.
- 1965 - 1968 Genetic Consultant, Hereditary Defects Unit, California State Department of Public Health.
- 1965 - Genetic Consultant, Congenital Malformations Branch, Epidemiology Section, Dental Health Center, U.S. Public Health Service.

Societies and Organizations

American Academy of Pediatrics
American Association of Poison Control Centers
American Federation for Clinical Research
American Public Health Association, Epidemiology Section
American Society of Human Genetics
Western Society for Pediatric Research

Specialty Board Certification

1960 American Board of Pediatrics

State and National Certification

Diplomate of National Board of Medical Examiners
Licensed to practice medicine in California and Colorado.

BIBLIOGRAPHY

1. Cann, H.M. and Herzenberg, L.A.: In Vitro Studies of Mammalian Somatic Cell Variation. I. Detection of H-2 Phenotype in Cultured Mouse Cell Lines, J. Exp. Med. 117:259, 1963.
2. Cann, H.M. and Herzenberg, L.A.: In Vitro Studies of Mammalian Somatic Cell Variation. II. Isoimmune Cytotoxicity With a Cultured Mouse Lymphoma and Selection of Resistant Variants. J. Exp. Med. 117:267, 1963.
3. Berrai, I. and Cann, H.M.: Segregation Analysis of Juvenile Diabetes Mellitus, J. Med. Genet. 2:8, 1965.
4. Cann, H.M.: Computer Analysis in Human Genetics: Segregation Analysis and Demographic Genetics, Ann. New York Acad. Sci. 126:728, 1965.
5. Barrai, I., Cann, H.M., Cavalli-Sforza, L.L. and DeNicola, P.: The Effect of Parental Age on Rates of Mutation for Hemophilia and Evidence for Differing Mutation Rates for Hemophilia A and B, American J. Hum. Genet. 20:175, 1968.
6. Cann, H.M. and Cavalli-Sforza, L.L.: Effects of Grandparental and Parental Age, Birth Order and Geographic Variation on the Sex Ratio of Liveborn and Stillborn Infants, American J. Hum. Genet., 20:381, 1968.
7. Cann, H.M.: Principles of Human Inheritance, in Human Genetics, Birth Defects, Original Article Series, The National Foundation, Vol. IV, November, 1968.

BIBLIOGRAPHY (Continued)

8. Cann, H.M., Van West, B., and Barnett, C.R.: Genetics of Diego Blood Groups in Guatemalan Indians: Use of Antiserums to Di^a and Di^b Antigens, Science, 162: 1391, 1968.
9. Greenstein, R.M., Harris, D.J., Luzzatti, L.L. and Cann, H.M.: Cytogenetic Analysis of a Boy with the XXXY Syndrome: Origin of the X-Chromosomes, Pediatrics, 45:677, 1970.
10. Dungy, C.I., Aptekar, R.G. and Cann, H.M.: Herediatry Hydrometrocolpos with Polydactyly in Infancy. Pediatrics, 47:138, 1971.
11. Barnett, C.R., Jackson, J. and Cann, H.M.: Childspacing in a Highland Guatemala Community, in Culture and Population: A Collection of Current Studies, Polgar, S. (ed.), Carolina Population Center, Univ. North Carolina, Chapel Hill, 1971.
12. Watson, W. and Cann, H.M.: Genetic Counseling in Dermatology. Pediat. Clin. N. America 18:757, 1971.
13. Watson, W., Cann, H.M., Farber, E. and Nall, L.: The Genetics of Psoriasis. Arch. Dermatol., In Press.
14. Bodmer, W.F., Bodmer, J.G., Coukell, A., Cann, H.M. and Van West, B.: Some Further Data on the Joint Segregation of HL-A and Haptoglobin. Ann. Hum. Genet. (London), In Press.

Book Review

Carter, C.O.: Human Heredity, Cytogenetics 2:55, 1963.

HONORS (Continued from Page 17)

1964	Society for Pediatric Research
1963 - 1968	Research Career Development Award, National Institutes of Health, U.S. Public Health Service
1962 - 1963	National Science Foundation Senior Postdoctoral Fellowship.